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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/027,654	02/23/98	HORTON J	28911/34561

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EXAMINER	
GABEL, G	
ART UNIT	**PAPER NUMBER**
1641	8

DATE MAILED: 03/15/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/027,654	Horton
Examiner	**Group Art Unit**
Gailene R. Gabel	1641

☒ Responsive to communication(s) filed on *Jan 11, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-18* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-18* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed January 11, 2000 is acknowledged and has been entered. Claims 1-13 have been amended. Claims 15-18 have been added. Claims 1-18 are pending and under examination.

Claim Rejections - 35 USC § 112

2. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as amended, remains indefinite in reciting "assaying for an analyte" in the preamble, in light of the addition of step (iv) because it is unclear what is encompassed by the term "assaying". Alternatively, since step (iv) denotes a qualitative step of "detecting the presence of ...", then the preamble may be clarified by reciting "assaying for the presence of an analyte in a sample". Such a language is suggested but not required.

Claim 1, step (I), remains indefinite in reciting "possibly containing the analyte" because the term "possibly" is a subjective term that lacks a comparative basis for defining its metes and bounds. Alternatively, in light of the addition of step (iv), cancellation of the phrase may obviate this rejection. Such a change is suggested but not required.

Claim 1, step (ii) remains indefinite in reciting "mixing... with assay reagents, including a specific binding partner" because it is unclear what is encompassed by the term "assay reagent". For example, does the assay reagent comprise a specific binding partner conjugated to a tracer or does the assay reagent comprise a tracer (only) which is added as a separate element from the specific binding partner that is included. It is unclear what the interactive structural and functional relationship is between the assay reagent and the specific binding partner. See also newly added claim 18.

Claim 1, step (iv) remains incomplete in failing to recite what is determined by detecting the presence of specific binding partner-analyte complex. For example, adding the statement "the presence of which is indicative of the presence of the analyte in the sample" is suggested but not required.

Claim 14 which recites a kit to perform the method of claim 1 is inconsistent and indefinite because it is unclear how the method can be practiced using the kit in claim 14 since claim 14 recites "a separation means for separating bound tracer from unbound tracer", but claim 1 to which it is dependent upon fails to recite such a separation as a method step . Accordingly, claim 1 omits essential steps and fails to recite a structural and functional element that is critical to the claimed invention.

Claim Rejections - 35 USC § 103

3. In light of applicant's argument, the rejection to claims 1-14 under 35 U.S.C. 103(a) as being unpatentable over Cook (1) (Research Focus, 1996) in view of Lundin (US 5,558,986) and in further view of Cook (2) (WO 94/26413) is, hereby, withdrawn.

4. Claims 1-4, 8-11, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook (1) (Research Focus, 1996) in view of Lundin (US 5,558,986) for reason of record.

5. Claims 1, 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cook (1) (Research Focus, 1996) in view of Lundin (US 5,558,986), and in further view of Cook (2) (WO 94/26413).

See Paper No. 6 for a thorough discussion of Cook (1), Lundin, and Cook (2).

Response to Arguments

6. Arguments to rejection of claims 1-4, 8-11 and 13-14:

(A) Applicant argues that the combined references of Cook (1) and Lundin to reject claims 1-4, 8-11 and 13-14 do not indicate that the lysis and specific binding reactions can successfully take place in a single reaction vessel such as taught by the instant invention.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the feature upon which applicant relies (i.e., single reaction vessel) is not recited in the rejected claims 1-4, 8-11 and 13-14.

(B) Applicant further argues that the there is no apparent or suggested motivation to combine the use of scintillation proximity assay as taught by Cook (1) and the sequestrant of Lundin. Applicant further argues that the combination of references does not teach the Applicant's invention. Applicants specifically contend that Lundin teaches extraction of components such as ATP, DNA, RNA for enzyme reaction and not for specific binding assays.

In response to applicant's argument (B) that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Cook (1) teaches scintillation proximity assay for biochemical and cellular targets which requires no separation and has been applied to various binding interactions which includes molecule binding, protein-peptide interactions, and cellular biochemistry assays. Cook (1) teaches immobilizing an analyte such as prostaglandin, interleukin, or adenosine-3',5'- cyclic monophosphate to a small scintillant-containing microsphere then binding tracers (radioisotopically labeled molecules) to the microsphere. Lundin was incorporated herein for his teaching in extracting intracellular analytes using a lysis reagent (dodecyl trimethyl ammonium bromide) and simultaneously contacting them with a sequestrant such as cyclodextrin to sequester the lysis reagent by forming a complex. The cyclodextrin is added always before or

simultaneously with the addition of specific binding partners. Lundin further discloses a kit for lysis and assay of analytes, i.e. ATP comprising a lysis reagent, a cyclodextrin, reagent with specific binding partner, and an assay buffer. One of ordinary skill in the art would have been motivated to combine the teaching of Lundin in extracting intracellular components and analytes as well as extractant neutralization with the method of scintillation proximity assay applications as taught by Cook (1) because Lundin specifically teaches efficient analyte separation and Cook (1) specifically teaches advantages of efficient separation such as convenience, ease, economy and safety from potential hazardous or radioactive materials due to minimal handling thereof. One of ordinary skill in the art would have reasonable expectation of success in acquiring optimal sequestrant concentration for use in neutralizing the lysis reagent because acquisition of optimal values and ranges is essential and standard practice in optimization procedures.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

7. Arguments to rejections of claims 1-14:

(A) Applicant argues that Cook (2) teaches away from the need to disrupt cells because applicants invention is based on lysis of cells and detection of intracellular analytes in a single

reaction vessel. Note withdrawal of rejection to claims 1-14 in No. 3 and new ground of rejection in No. 5 in page 4 of this action.

Cook (2) was incorporated into the combination of references for his teaching in the capacity of each individual vessel in the multiwell of his invention to allow cell growth in culture medium and then subjecting the elements to cellular studies which includes binding and movement between scintillating layers in the same individual vessel in the multiwell. Contrary to applicant's contention, Cook (2) reference is applicable in his teaching of intracellular biological activity and ligand interactions (see pages 10, 14 and 17). Lundin was incorporated herein for his teaching in extracting intracellular analytes using a lysis reagent (dodecyl trimethyl ammonium bromide) and simultaneously contacting them with a sequestrant such as cyclodextrin to sequester the lysis reagent by forming a complex. By lysing cells to access and expose analytes, detection and quantitation thereof can be better effected.

(B) Applicant further argues that the there is no apparent or suggested motivation to combine the use of scintillation proximity assay as taught by Cook and the sequestrant of Lundin. Applicant further argues that the combination of references does not teach the Applicant's invention.

In response to applicant's argument (B) that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some

teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Cook (2) teaches studying cellular processes by introducing into a vessel a sample of cells labeled with a radioisotope emitting electrons, and using detection means to observe scintillation. The multiwell plate can take various formats for the purpose of culturing cells using standard cell culture media and growing cells in a sterile environment. It would have been obvious to one of ordinary skill in the art to incorporate that use of a multiwell system with an array of reaction vessels as taught by Cook (2) into the teachings of Cook (1) and Lundin supra because it allows for minimal handling of materials in high-throughput immunoassay testing and Cook (1) specifically teaches the need for rapid, high flux simultaneous homogeneous assays and incorporation of derivatized multiwell systems capable of cellular growth as taught by Cook (2) accounts for high capacity yet efficient system achievable in assaying a wide variety of biochemical and cellular analytes for screening and identification.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

8. Applicant's amendment and arguments have been considered but not deemed persuasive. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gail Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

3-10-00

Gail Gabel
Patent Examiner
Group 1641

3/13/00

JAMES C. HOUSEL
SUPERVISORY PATENT EXAMINER